

WEST Search History

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DATE: Thursday, August 12, 2004

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L1	tamura-T\$.in.	8505
<input type="checkbox"/>	L2	oto-N\$.in. or suzuki-N\$.in. or mizuno-K\$.in.L1	12547
<input type="checkbox"/>	L3	oto-N\$.in. or suzuki-N\$.in. or mizuno-K\$.in.	16755
<input type="checkbox"/>	L4	yamamoto-N\$.in. or suzuki-N\$.in. or mizuno-K\$.in.	23444
<input type="checkbox"/>	L5	(l1 or l4) and (biochip or array)	640
<input type="checkbox"/>	L6	(l1 or l4) and (biochip or microarray or array)	653
<input type="checkbox"/>	L7	L6 and hybridiz\$	55
<input type="checkbox"/>	L8	L7 and biopolymer	17
<input type="checkbox"/>	L9	l8 and visual\$	6
<input type="checkbox"/>	L10	probe similarity score	0
<input type="checkbox"/>	L11	similarity score	958
<input type="checkbox"/>	L12	biochip or microarray	13969
<input type="checkbox"/>	L13	L12 same biopolymer	1
<input type="checkbox"/>	L14	l11 and l12	47
<input type="checkbox"/>	L15	L14 and biopolymer	11
<input type="checkbox"/>	L16	L15 and (imag\$ and visual\$)	7
<input type="checkbox"/>	L17	L16 and hybridiz\$	7
<input type="checkbox"/>	L18	l12 and biopolymer	1324
<input type="checkbox"/>	L19	L18 and hybridiz\$	1188
<input type="checkbox"/>	L20	L19 and (similar\$ scor\$ or percent homology or percent identity or sequence identity)	443
<input type="checkbox"/>	L21	L20 and (display\$ and imag\$ and visual\$)	271
<input type="checkbox"/>	L22	L21 and (different same color)	19
<input type="checkbox"/>	L23	L22 and (different same (valu\$ or depth))	14
<input type="checkbox"/>	L24	L23 and spot imag\$	1
<input type="checkbox"/>	L25	L23 and statistic\$	14
<input type="checkbox"/>	L26	L25 and matrix	12
<input type="checkbox"/>	L27	L26 and (hybridization level or hybridization profile)	1
<input type="checkbox"/>	L28	L25 and storage unit	1
<input type="checkbox"/>	L29	L25 and (data near storage)	6

<input type="checkbox"/>	L30	L25 and hybridization	14
<input type="checkbox"/>	L31	((biopolymer or probe) near (biochip or microarray))	161
<input type="checkbox"/>	L32	L31 and ((display\$ or visual\$) same hybridiz\$)	12
<input type="checkbox"/>	L33	(display\$ or visual\$) same (percent identity or percent homology or sequence identity or sequence similarity or similarity score)	2672
<input type="checkbox"/>	L34	L33 same (hybridization)	94
<input type="checkbox"/>	L35	L34 and (graphic\$)	6
<input type="checkbox"/>	L36	L33 and (different near color)	48
<input type="checkbox"/>	L37	L36 and (image)	31
<input type="checkbox"/>	L38	l31 and l33	18
<input type="checkbox"/>	L39	(display\$ or visual\$)near(percent identity or percent homology or sequence identity or sequence similarity or similarity score)	119
<input type="checkbox"/>	L40	L39 and hybridiz\$	92
<input type="checkbox"/>	L41	L40 and (biochip or microarray)	20
<input type="checkbox"/>	L42	L41 and (biopolymer or probe)	20
<input type="checkbox"/>	L43	L39 and (biochip or microarray)	20
<input type="checkbox"/>	L44	L33 and (biochip or microarray)	416
<input type="checkbox"/>	L45	L44 and hybridization	387
<input type="checkbox"/>	L46	L45 and ((Imag\$ or matrix or graphic\$) same (different near color))	1
<input type="checkbox"/>	L47	L45 and ((Imag\$ or matrix or graphic\$) and (different near color))	6
<input type="checkbox"/>	L48	BLAST same (imag\$ or graphic\$ or visual\$)	4055
<input type="checkbox"/>	L49	L48 same (biochip or micrarray)	4
<input type="checkbox"/>	L50	6188783.pn. or 5812272.pn. or 6471916.pn. or 6284465.pn.	8
<input type="checkbox"/>	L51	6349144.pn. or 4852183.pn. or 6306643.pn. or 6228575.pn.	8

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 15:37:26 ON 12 AUG 2004)

FILE 'STNGUIDE' ENTERED AT 15:37:29 ON 12 AUG 2004

FILE 'HOME' ENTERED AT 15:37:33 ON 12 AUG 2004

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 15:37:44 ON 12 AUG 2004

L1 44945 S TAMURA T?/AU OR YAMAMOTO N?/AU OR SUZUKI N?/AU
L2 67910 S BIOCHIP OR MICROARRAY
L3 82 S L1 AND L2
L4 2 S L3 AND (BIOPOLYMER AND PROBE)
L5 55 DUP REM L3 (27 DUPLICATES REMOVED)
L6 0 S L5 AND (SIMILARITY SCORE OR PERCENT HOMOLOGY OR PERCENT ID)
L7 23 S L2 AND (BIOPOLYMER AND PROBE)
L8 18 S L7 AND HYBRIDIZ?
L9 17 DUP REM L8 (1 DUPLICATE REMOVED)
L10 6416 S L2 AND (IMAG? OR VISUAL? OR DISPLAY?)
L11 1933 S L10 AND HYBRIDIZATION
L12 184 S L11 AND (SIMILARITY OR HOMOLOGY OR IDENTITY)
L13 0 S L12 AND (DIFFERENT (5A) COLOR)
L14 8 S L12 AND COLOR
L15 2 DUP REM L4 (0 DUPLICATES REMOVED)
L16 157 DUP REM L12 (27 DUPLICATES REMOVED)
L17 8 S L16 AND GRAPHIC?
L18 8 DUP REM L17 (0 DUPLICATES REMOVED)
L19 7 S L16 AND (STATISTIC?)
L20 7 DUP REM L19 (0 DUPLICATES REMOVED)

=>

=> d ibib abs 116 17 33 37 42 43 46 47 124 139 141

L16 ANSWER 17 OF 157 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-15594 BIOTECHDS

TITLE: Concurrent interrogation of a number of polymorphic sites, useful for genetic testing, carrier screening, genetic profiling, and **identity** testing, comprises conducting a multiplexed elongation assay using probes; for use in polymorphism detection and expression profiling

AUTHOR: LI A X; HASHMI G; SEUL M

PATENT ASSIGNEE: BIOARRAY SOLUTIONS LTD

PATENT INFO: WO 2003034029 24 Apr 2003

APPLICATION INFO: WO 2002-US33012 15 Oct 2002

PRIORITY INFO: US 2002-364416 14 Mar 2002; US 2001-329427 15 Oct 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-393553 [37]

AN 2003-15594 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Concurrent interrogation of a number of polymorphic sites, comprises conducting a multiplexed elongation assay by: (a) applying one or more temperature cycles to achieve linear amplification of the target; or (b) a combination of annealing and elongation steps under temperature-controlled conditions.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a method of concurrent determination of nucleotide composition at designated polymorphic sites located within one or more target nucleotide sequences; (2) methods of sequence-specific amplification of assay signals produced in the analysis of a nucleic acid sequence of interest in a biological sample; (3) a method of forming a covering probe set for the concurrent interrogation of a designated polymorphic site located in one or more target nucleic acid sequences; (4) methods of identifying or determining polymorphisms at one or more, or two or more, designated sites of a target nucleotide sequence or within a target polynucleotide sequence; (5) a method of concurrent interrogation of a nucleotide composition at S polymorphic sites, $P_{\text{sub}} S = (c_{\text{sub}} P_{\text{sub}} (s); 1 \text{ at most } s \text{ at most } S)$ located within one or more contiguous target sequences; (6) a method of concurrently determining a configuration of multiple designated sites in one or more targets; (7) a method of determining a configuration of at least one designated site in one or more nucleic acids; (8) a method for the concurrent interrogation of a set of designated polymorphisms within one or more nucleic acids; (9) methods of determining a sequence of a nucleic acid; (10) methods of determining a sequence of at least one designated site in one or more nucleic acids; (11) a kit for determining the sequence of designated polymorphic sites of a nucleic acid comprising several probes, where each probe contains a terminal elongation initiation region that is designed to align with a portion of the nucleic acid at the designated site and that is capable of initiating an elongation of the probe, and a variable duplex anchoring region designed to align with different portions of the nucleic acid; (12) a method of amplifying a nucleic acid; (13) a method of determining the composition of polymorphic sites in a nucleic acid; (14) methods of detecting an elongation reaction; and (15) probes selected from the group of probes listed in the specification.

BIOTECHNOLOGY - Preferred Kit: The probes are formed into an encoded array or probes. The kit further comprises means for performing an assay to anneal the probes to the nucleic acid, and the assay further comprises a means for elongating the annealed probes. The kit also comprises means for detecting which probes are elongated. Preferred Method: Concurrent determination of nucleotide composition at designated polymorphic sites located within one or more target nucleotide sequences comprises: (a) providing one or more sets of probes, each probe capable of annealing to

a subsequence of target nucleotide sequence(s) located within a range of proximity to a designated polymorphic site; (b) contacting the set of probes with the target nucleotide sequences to permit formation of **hybridization** complexes by placing an interrogation site within a probe sequence in direct alignment with the designated polymorphic site; (c) determining the presence of a match or a mismatch between the interrogation site and a designated polymorphic site, for each **hybridization** complex; and (d) determining the composition of the designated polymorphic site. The target nucleotide sequences are produced in a multiplex PCR reaction using one or more primer sets. The primer sets are degenerate primer sets. The targets are fragments of genomic DNA or of cDNA. The probes are spatially encoded on a substrate, or immobilized on encoded microparticles. The encoded microparticles are assembled into a random encoded array. Each probe contains a terminal elongation initiation region capable of initiating an elongation or extension reaction. The reaction is catalyzed by a polymerase lacking 3'-5' exonuclease activity. Determining the presence of a match or a mismatch comprises adding one or more deoxynucleotide triphosphates, where the method further comprises using a polymerase capable of extending or elongating probes. At least one of the deoxynucleotide triphosphates is labeled to generate an optically detectable signature associated with the elongation product. An optical label is attached to one or more probes by annealing to the probes a fluorescently labeled target to form a fluorescent **hybridization** complex. The method further comprises using a polymerase capable of extending or elongating probes **displaying** a match by addition of one or more deoxynucleotide triphosphates to form an elongated **hybridization** complex, and identifying elongation products by detecting the stability of optical signatures under conditions in which temperature is set to a value above the melting temperature of any **hybridization** complex formed by target and non-matched probe but below the melting temperature of any extended **hybridization** complex formed by target and elongated probe. One or more probes from the set of probes are immobilized on encoded microparticles and a change in optical signature is detected. The arrays are arranged in a spatially encoded manner. The change in optical signature is detected and particle **identity** is determined. Sequence-specific amplification of assay signals produced in the analysis of a nucleic acid sequence of interest in a biological sample comprises: (a) providing a set of immobilized probes capable of forming a **hybridization** complex with the sequence of interest; (b) contacting the set of immobilized probes with the biological sample containing the sequence of interest under conditions which permit the sequence of interest to anneal to at least one of the immobilized probes to form a **hybridization** complex; (c) contacting the **hybridization** complex with a polymerase to allow elongation or extension of the probes contained within the **hybridization** complex; (d) converting elongation or extension of the probes into an optical signal; and (e) recording the optical signal from the set of immobilized probes in real time. The method further comprises performing one or more cycles, each cycle comprising annealing-extending/elongating-detecting-denaturing steps, where each cycle results in the increase of the number of extended or elongated probes in arithmetic progression. The method comprises setting a first temperature favoring the formation of a **hybridization** complex, setting a second temperature favorable to polymerase-catalyzed extension, converting extension or elongation into optical signal, recording/**imaging** optical signal/signatures from all probes, and setting a third temperature to ensure denaturation of all **hybridization** complexes. Sequence-specific amplification of assay signals produced in the analysis of a nucleic acid sequence of interest in a biological sample, where the method permits real-time monitoring of amplified signal, comprises: (a) providing a temperature-controlled sample containment device with associated temperature control apparatus permitting real-time recording of optical assay signal produced within the device; (b) providing within the sample

containment device a set of distinguishable, immobilized oligonucleotide probe capable forming a **hybridization** complex with the sequence of interest; (c) permitting the sequence to anneal to the set of immobilized oligonucleotide probes to form a **hybridization** complex; (d) contacting the **hybridization** complex with a polymerase to allow elongation of extension of the matched probes contained within a **hybridization** complex; (e) providing means to convert elongation or extension of matching probes into an optical assay signal; (f) providing an optical recording/**imaging** device capable of recording optical assay signals from the set of immobilized probes in real time; (g) performing one or more annealing-extending-detecting-denaturing cycles, each cycle increasing the number of extended or elongated probes in arithmetic progression. Forming a covering probe set for the concurrent interrogation of a designated polymorphic site located in one or more target nucleic acid sequences comprises: (a) determining the sequence of an elongation probe capable of alignment of the interrogation site of the probe with a designated polymorphic site; (b) further determining a complete set of degenerate probes to accommodate all non-designated as well as non-selected designated polymorphic sites while maintaining alignment of the interrogation site of the probe with the designated polymorphic site; and (c) reducing the degree of degeneracy by removing all tolerated polymorphisms. The covering set contains at least two probes with different interrogation site composition per designated site. The reduction of complexity is accomplished by probe pooling. Identifying polymorphisms at one or more designated sites on one or more target nucleotides comprises: (a) providing one or more probes capable of interrogating the designated sites; (b) forming an elongation product by elongating one or more probes designed to interrogate a designated site; and (c) determining the compositions at two or more sites. The method further comprises forming a **hybridization** complex by annealing to the elongation product a second probe designed to interrogate a second designated site. Identifying polymorphisms at one or more designated sites within a target polynucleotide sequence comprises providing one or more probes capable of interrogating the designated sites, assigning a value to each designated site while accommodating non-designated polymorphic sites located within a range of proximity to each polymorphism. The **homology** between the probes and the target sequence is analyzed by multiplexing. Determining polymorphisms at one or more designated sites of a target nucleotide sequence comprises providing one or more pairs of probes capable of detecting deletions, where the deletions are placed at the 3' terminus of the probe or within 3-5 bases of the 3' terminus. Alternatively, the method comprises providing a probe set for the designated sites and grouping the probe set in different probe subsets according to the terminal elongation initiation of each probe. The method further comprises multiplexing the probe set, measuring each probe in the probe set without interference from the other probes in the probe set and changing the allele matching pattern of a target polynucleotide sequence to include alleles that are tolerated by a probe set. Changing the allele matching pattern of a target polynucleotide sequence comprises pooling one or more probe sets to include matched allele, or comparing the signal intensities produced by the probe set. The method further comprises separating the terminal elongation initiation region and duplex anchoring region on the probe set. Identifying polymorphisms at two or more designated sites of a target nucleotide sequence comprises selecting a multiplicity of designated polymorphic sites to permit allele assignment, providing two or more probes capable of concurrent interrogation of the multiplicity of designated sites, assigning a value to each designated site, and combining the values to determine the **identity** of an allele or group of alleles while accommodating non-designated sites near the designated polymorphisms. Concurrent interrogation of a nucleotide composition at S polymorphic sites, $P_{\text{sub } S} = (c_{\text{sub } P} (s); 1 \text{ at most } s \text{ at most } S)$ located within one or more contiguous target sequences comprises assigning to each $c_{\text{sub } P}$ one of a limited set of possible

values by performing the following steps: (a) providing a set of designated immobilized oligonucleotide probes, also known as elongation probes, each probe capable of annealing in a preferred alignment to a subsequence of the target located proximal to a designated polymorphic site, the preferred alignment placing an interrogation site within the probe sequence in direct juxtaposition to the designated polymorphic site, the probes further containing a terminal elongation initiation (TEI) region capable of initiating an elongation or extension reaction; (b) permitting the target sequences to anneal to the set of immobilized oligonucleotide probes to form probe-target **hybridization** complexes; and (c) for each probe-target **hybridization** complex, calling a match or a mismatch in composition between interrogation site and corresponding designated polymorphic site. The probes are immobilized in a spatially encoded fashion on a substrate, or on encoded microparticles, which are assembled in a random encoded array on a substrate. The calling step involves the use of a polymerase capable of extending or elongating probes whose interrogation site composition matches that of the designated polymorphic site in the target, and only those probes, by addition of one or more nucleoside triphosphates, one of which is labeled to generate an optically detectable signature. The probes are immobilized on encoded microparticles and the change in optical signature is detected, and particle **identity** determined, by flow cytometry or by direct **imaging**.

Concurrently determining a configuration of multiple designated sites in one or more targets comprises: (a) providing primers for amplification of the target(s), providing a probe array, using the probe array to perform an assay that produces an elongation product; and (b) detecting the elongation product. Determining a configuration of at least one designated site in one or more nucleic acids comprises: (a) providing several copies of one or more nucleic acids, each nucleic acid having at least one polymorphism; (b) choosing at least one polymorphism as a designated site; (c) providing two or more types of probes capable of concurrently interrogating each designated site to determine a composition of each designated site; (d) contacting the probes to the copies of one or more nucleic acids under conditions that cause at least some probes to hybridize to the nucleic acids; (e) performing an elongation reaction that elongates members of the probe set that are annealed to the nucleic acid; (f) detecting the elongation reaction; and (g) assigning a value to each designated site. Each type of probe comprises a terminal elongation region that is designed to align with a portion of the nucleic acid at the designated site and that is capable of initiating a polymerase-catalyzed elongation of the probe, and a variable duplex anchoring region designed to align with different portions of the nucleic acid. The method further comprises combining the values to determine the **identity** of each designated site. The value assigned to the designated site corresponds to the nucleotide **identity** at the designated site. The value assigned to the designated site corresponds to a 1 if the probe perfectly matches the nucleic acid and a 0 if the probe does not perfectly match the nucleic acid. The values are combined to determine the **identity** of an allele or group of alleles. The terminal elongation initiation region is immediately adjacent to the duplex anchoring region, or is linked to the duplex anchoring region by a molecular tether. The duplex anchoring regions of the probes in the probe set are designed to take into account polymorphism in non-designated sites. The nucleic acids are obtained from the cystic fibrosis conductance transmembrane regulator (CFTR) gene or the human leukocyte antigen (HLA) gene. The probes align with a target sequence of a sense or antisense DNA strand. **Homology** between the probes and the target sequence is analyzed in parallel reactions. At least one polymorphism is a deletion, an insertion, or a single nucleotide polymorphism. Each probe is designed to detect deletions, where the portion is at the 3' terminus or within 3-5 bases of the 3' terminus. Probes with the same terminal elongation region are grouped together. Concurrent interrogation of a set of designated polymorphisms

within one or more nucleic acids comprises: (a) providing several copies of one or more nucleic acids, which contain a set of designated polymorphisms; (b) contacting the nucleic acids to several types of probes, where each type of probe is capable of annealing to the nucleic acid(s) and has a different length than the other types of probes; (c) annealing the nucleic acid(s) to the probes; (d) elongating the probes; (e) detecting the elongated probes; and (f) determining the sequence of the designated polymorphism in the nucleic acid. Determining a sequence of a nucleic acid comprises providing several copies of nucleic acids having at least one polymorphism, choosing at least one polymorphism as a designated site, providing several types of probes cited above, where the probes are coupled to one or more solid supports, and performing an assay to determine a sequence of the nucleic acid. Determining a sequence of at least one designated site in one or more nucleic acids comprises: (a) providing a buffer solution comprising several copies of one or more nucleic acids having polymorphic sites, with at least one polymorphic site chosen as a designated site, two or more types of probes, a polymerase, and several types of dNTPs, where at least one type of dNTP is labeled; (b) heating the buffer solution to a first temperature to cause annealing of the probes to the nucleic acid(s); (c) heating the buffer solution to a second temperature to cause elongation of the annealed probes; and (d) detecting the elongated probes to determine the sequence of the designated sites of the nucleic acids. Amplifying a nucleic acid comprises providing several types of probes that are coupled to several types of encoded beads, where each type of probe is coupled to only one type of encoded bead, providing a template molecule capable of annealing to at least one type of probe, performing at least one cycle of amplification, which comprises annealing the template to at least one type of probe, elongating the annealed probes, and denaturing annealed template. Determining the composition of polymorphic sites in a nucleic acid comprises: (a) providing a nucleic acid having polymorphic sites; (b) choosing at least two polymorphic sites as designated sites; (c) providing two or more probes capable of interrogating the designated sites; (d) interrogating the designated sites so that the presence of the designated sites is established and compositions at the sites are determined. Interrogating the designated sites comprises: (a) forming a **hybridization** complex between a first probe and the nucleic acid; (b) forming an elongation product by elongating the first probe; and (c) forming a **hybridization** complex by annealing to the elongation product a second probe designed to interrogate a second designated site. One or more **hybridization** steps at additional designated sites follow the **hybridization** step. Detecting an elongation reaction comprises: (a) providing several probes; (b) coupling the probes to encoded beads that permit the identification of the probes; (c) contacting the encoded beads with a solution containing nucleic acids and dATP, dCTP, dTTP, and dGTP, where one type of the dNTPs comprises a label, or with a solution containing one labeled ddNTP and three dNTPs; (d) providing a polymerase; (e) performing an elongation reaction; and (f) detecting a product of an elongation reaction. The label is a fluorescent tag. Alternatively, the method comprises providing several probes, coupling the probes to encoded beads that permit the identification of the probes, contacting the encoded beads with a solution containing dATP, dCTP, dTTP, and dGTP, providing a polymerase, performing an elongation reaction to obtain an elongated probe, providing a labeled oligonucleotide probe designed to be complementary to a portion of the elongated probe, annealing the probe to the elongated probe, and detecting the elongated probe. The method may also comprise: (a) providing a labeled target sequence, providing several types of probes, where one type of probes is exactly complementary to the labeled target sequence; (b) coupling the probes to encoded beads that permit the identification of the types of probes; (c) annealing the labeled target to the probes; (d) performing an elongation reaction to obtain elongated probes; (e) heating annealed probes to a temperature, the temperature being sufficient to denature duplex structures containing probes that do

not match while preserving duplex structures corresponding to perfectly matched probes; and (f) identifying the elongation product corresponding to perfectly matched probes by determining which encoded beads have a bound target sequence after heating.

USE - The probes and methods are useful for identifying or detecting polymorphisms at one or more designated sites. The methods are useful for identifying mutations within the cystic fibrosis conductance transmembrane regulator (CFTR) or the human leukocyte antigen (HLA) gene. Concurrent interrogation of a multiplicity of polymorphic sites is useful for genetic testing, carrier screening, genotyping or genetic profiling, and **identity** testing. The methods are also useful for improving the reliability and accuracy of polymorphism analysis of target regions containing polymorphic sites in addition to the polymorphic sites designated for interrogation.

EXAMPLE - Genomic DNA, extracted from several patients, was amplified with corresponding primers in a multiplexed polymerase chain reaction (PCR) (mPCR). Following amplification, products were purified to remove all reagents using a commercially available kit. DNA concentration was determined by spectrophotometric analysis. Single or pooled PCR products (20 ng each) were added to an annealing mixture containing 10 mM Tris-hydrochloric acid, 1 mM ethylene diamine tetraacetic acid (EDTA), 0.2 M sodium chloride, 0.1% Triton X-100. The annealing mixture was mixed with elongation mixture containing 3 U of thermo sequenase, 1 x enzyme buffer with fluorescein-labeled or TAMRA-labeled dNTP analogs and 1-10 micromole of each type of unlabeled dNTP and placed in contact with an array of oligonucleotide probes **display** on a color-coded array. The annealing and elongation reactions were allowed to proceed in a temperature-controlled cycler. The temperature steps were three minutes each at 65 degreesC, 60 degreesC, 55 degreesC, 50 degreesC and 45 degreesC, with a ramp between temperatures of less than 30 seconds. The bead array was washed with distilled water for 5-15 minutes and an **image** containing the fluorescence signal from each bead within the array was recorded using a fluorescence microscope equipped with a CCD camera. **Images** were analyzed to determine the **identity** of each of the elongated probes. (143 pages)

L16 ANSWER 33 OF 157 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-19646 BIOTECHDS

TITLE: Internet-based DNA analysis support system has secondary database to store data beforehand obtained by searching **homology** in base-sequence database based on probe sequence of DNA-chip probe;
computer bioinformatic software and hardware useful for DNA analysis

PATENT ASSIGNEE: SUMITOMO SEIYAKU KK

PATENT INFO: JP 2003058548 28 Feb 2003

APPLICATION INFO: JP 2001-250276 21 Aug 2001

PRIORITY INFO: JP 2001-250276 21 Aug 2001; JP 2001-250276 21 Aug 2001

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: WPI: 2003-516721 [49]

AN 2003-19646 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A secondary database (10) in a web server (1) stores the data beforehand obtained by searching **homology** in base-sequence database based on the probe sequence of a DNA-chip probe. A search software (12) searches a probe sequence name with respect to the secondary database and **displays** the retrieval result.

USE - The database is useful for an Internet-based DNA analysis support system.

ADVANTAGE - The DNA analysis can be performed efficiently in short time. (9 pages)

L16 ANSWER 37 OF 157 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS

RESERVED. on STN
ACCESSION NUMBER: 2004216772 EMBASE
TITLE: cDNA **microarray** detection of 208 lung
cancer-related genes in seven samples of lung squamous cell
carcinoma.
AUTHOR: Fan B.-X.; Sun J.-F.; Xie L.-X.; Chen L.-A.; Liu Y.-N.;
Wang S.-Q.; Wu D.-C.
CORPORATE SOURCE: B.-X. Fan, Department of Respiratory Disease, 301 Hospital
of PLA, Beijing 100853, China. fanbx@263.net.cn
SOURCE: Chinese Journal of Clinical Rehabilitation, (2003) 7/32
(4320-4321).
Refs: 11
ISSN: 1671-5926 CODEN: ZLKHAH
COUNTRY: China
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English; Chinese
AB Aim: To investigate the differences in the expressions of lung
cancer-related genes in seven tissue specimens of lung squamous cell
carcinoma by means of cDNA **microarray** technique, so as to
provide molecular information for the treatment and prognostic assessment
of the patients. Methods: The total RNA of 7 lung squamous cell carcinomas
tissues samples was extracted, reverse transcribed and
fluorescent-labeled to be used as probes through LD-PCR.
Hybridization of the probes with the cDNA chip that contained 208
lung cancer-related genes was performed, the results analyzed using
imagine software. Results: The 7 samples share a
similarity ranging from 60.65% to 82.69% in the expressions of 208
lung cancer-related genes. Conclusion: It is identified for the first time
that the gene expression profiles might differ in certain aspect among
different lung squamous cell carcinomas, a fact that justifies more
individualized diagnosis and treatment of the cancer patients.

L16 ANSWER 42 OF 157 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
DUPLICATE 2
ACCESSION NUMBER: 2003-28464 BIOTECHDS
TITLE: Quantitative comparison of cDNA-AFLP, microarrays, and
GeneChip expression data in *Saccharomyces cerevisiae*;
DNA array, **biochip** and amplified length fragment
polymorphism comparison useful for gene expression
analysis
AUTHOR: REIJANS M; LASCARIS R; GROENEGER AO; WITTEBERG A; WESSELINK
E; VAN OEVEREN J; DE WIT E; BOORSMA A; VOETDIJK B; VAN DER
SPEK H; GRIVELL LA; SIMONS G
CORPORATE SOURCE: Keygene NV; Univ Amsterdam
LOCATION: Simons G, Keygene NV, NL-6700 AE Wageningen, Netherlands
SOURCE: GENOMICS; (2003) 82, 6, 606-618
ISSN: 0888-7543
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 2003-28464 BIOTECHDS
AB AUTHOR ABSTRACT - cDNA-AFLP is a genome-wide expression analysis
technology that does not require any prior knowledge of gene sequences.
This PCR-based technique combines a high sensitivity with a high
specificity, allowing detection of rarely expressed genes and
distinguishing between homologous genes. In this report, we validated
quantitative expression data of 110 cDNA-AFLP fragments in yeast with DNA
microarrays and GeneChip data. The best correlation was found between
cDNA-AFLP and GeneChip data. The cDNA-AFLP data revealed a low number of
inconsistent profiles that could be explained by gel artifact,
overexposure, or mismatch amplification. In addition, 18 cDNA-AFLP

fragments displayed homology to genomic yeast DNA, but could not be linked unambiguously to any known ORF. These fragments were most probably derived from 5' or 3' noncoding sequences or might represent previously unidentified ORFs. Genes liable to cross **hybridization** showed identical results in cDNA-AFLP and GeneChip analysis. Three genes, which were readily detected with cDNA-AFLP, showed no significant expression in GeneChip experiments. We show that cDNA-AFLP is a very good alternative to microarrays and since no preexisting biological or sequence information is required, it is applicable to any species. (C) 2003 Elsevier Inc. All rights reserved. (13 pages)

L16 ANSWER 43 OF 157 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003330830 EMBASE

TITLE: Quantitative analysis of colorectal tissue microarrays by immunofluorescence and *in situ hybridization*.

AUTHOR: Jubb A.M.; Landon T.H.; Burwick J.; Pham T.Q.; Frantz G.D.; Cairns B.; Quirke P.; Peale F.V.; Hillan K.J.

CORPORATE SOURCE: A.M. Jubb, Genentech Inc, Department of Pathology, 1 DNA Way, South, San Francisco, CA 94080, United States.
adrianj@gene.com

SOURCE: Journal of Pathology, (1 Aug 2003) 200/5 (577-588).
Refs: 59
ISSN: 0022-3417 CODEN: JPTLAS

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
029 Clinical Biochemistry
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The accuracy and reliability of *in situ* studies may be compromised by qualitative interpretations. Quantitation imposes a greater degree of objectivity, is more reproducible, and facilitates the clarity of definitions. The aim of this study was to validate the utility of laser **imaging** systems for the *in situ* quantitative analysis of gene expression in tissue microarrays. Immunofluorescence was employed to quantify the expression of the tumour suppressor p53, a marker of proliferation (Ki67), an endothelial cell marker (CD31), and the mismatch repair proteins human Mut L homologue 1 and human Mut S homologue 2 in an arrayed series of colorectal tissues (n = 110). Quantitative data on this panel of antigens were compared objectively with qualitative scoring of immunohistochemical chromogen deposition. In addition, the expression of vascular endothelial growth factor (VEGF)-A, placental growth factor, hepatocyte growth factor, and c-Met mRNA was quantified by phosphor **image** analysis of *in situ hybridization* reactions. The quantified data on p53, Ki67, and CD31 expression were significantly associated with the pathologist's score ($P \leq 0.001$). While hepatocyte growth factor and placental growth factor were not up-regulated, c-Met expression was increased up to 2.5-fold and the median VEGF-A expression was elevated 4-fold ($p = 0.003$) in this series of colorectal tumours. Laser **imaging** systems are therefore feasible for high-throughput, quantitative profiling of tissue microarrays.
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L16 ANSWER 46 OF 157 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003201348 EMBASE

TITLE: Plant virus cDNA chip **hybridization** for detection and differentiation of four cucurbit-infecting tobamoviruses.

AUTHOR: Lee G.P.; Min B.E.; Kim C.S.; Choi S.H.; Harn C.H.; Kim S.U.; Ryu K.H.

CORPORATE SOURCE: K.H. Ryu, Plant Virus GenBank, College of Natural Science, Seoul Women's University, Seoul 139-774, Korea, Republic of. ryu@swu.ac.kr
SOURCE: Journal of Virological Methods, (9 Jun 2003) 110/1 (19-24).
Refs: 16
ISSN: 0166-0934 CODEN: JVMEDEH
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A plant virus cDNA chip was developed by using viral cDNA clones and **microarray** technology. The cDNA chip was designed for detection and differentiation of the four species of selected cucurbit-infecting tobamoviruses [target viruses: Cucumber green mottle mosaic virus (CGMMV); Cucumber fruit mottle mosaic virus (CFMMV); Kyuri green mottle mosaic virus (KGMMV); and Zucchini green mottle mosaic virus (ZGMMV)]. The chip consisted of cDNA clones of the four cucurbit-infecting tobamoviruses, two target-related tobamoviruses, and another three unrelated plant viruses. Polymerase chain reaction products were amplified from the selected cDNA clones and arrayed onto slide glass. The cDNA chip, which was called cucurbit-virus chip, detected successfully specific target viruses. When applied to probes made from ZGMMV-infected samples, ZGMMV reacted strongly with its homologous cDNA and moderately reacted with KGMMV and CFMMV, while it did not react with CGMMV on the same chip. CGMMV probe gave strong signal intensity to its homologous cDNA spot and weakly reacted with ZGMMV, KGMMV, and CFMMV. The signal intensity of all combinations of probe and target was correlated significantly with nucleotide sequence identities between the probes and target viruses based on scatter diagrams. The signals could be made as **image** files for specific virus detection, and this could be useful for virus identification and differentiation. This is the first report of plant virus detection by using cDNA chip technology. .COPYRGT. 2003 Elsevier Science B.V. All rights reserved.

L16 ANSWER 47 OF 157 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:545533 BIOSIS

DOCUMENT NUMBER: PREV200300546747

TITLE: A new screening system with **microarray** technology for signature tagged mutagenesis with *Desulfovibrio* and *Shewanella*.

AUTHOR(S): Luo, Q. [Reprint Author]; Steger, J. L. [Reprint Author]; Smalley, D. J. [Reprint Author]; Ballard, J. D. [Reprint Author]; Krumholz, L. R. [Reprint Author]

CORPORATE SOURCE: University of Oklahoma, Norman, OK, USA

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. Q-362. <http://www.asmusa.org/mtgsrc/generalmeeting.htm>. cd-rom. Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology.

ISSN: 1060-2011 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 19 Nov 2003

Last Updated on STN: 19 Nov 2003

AB Sulfate-reducing bacteria (SRB) are widely distributed in aquatic and terrestrial sediments. Signature tagged mutagenesis (STM) is a powerful technique that can be used to identify genes expressed by bacteria during exposure to conditions in their natural environments. To date, there are no reports where this approach has been used to study environmental microorganisms. We have recently identified pBSL180 containing a modified Tn10 which efficiently transforms *Desulfovibrio desulfuricans* G20 and

Shewanella oneidensis MR1 and produced stable transformants. STM requires the presence of oligonucleotide tags within the transposon ultimately used to identify mutants. To generate the tagged transposon system, random tags with a 40 base pair variable region and flanking 20 base pair constant arm were designed. Here we demonstrate a new screening system with **microarray** technology in place of blot analysis to **visualize** surviving tags and to identify genes that are required for sediment survival. We optimized the concentration of target DNA, concentration of probe, probe labeling reaction, **hybridization** conditions, and washing conditions. Results showed that spots produced using 14 mug/mul of 40 bp DNA provided optimal target DNA concentration on poly-L- lysine treated slides. The indirect labeling method for probes was more efficient and less costly than the direct labeling method. Optimization of washing stringency was crucial to decrease background signal, while maintaining a high intensity of specific **hybridization**. Washing buffer (0.2XSSC/0.2%SDS) preheated to 55degreeC and washed at room temperature provided ideal conditions. Cross **hybridization** was observed with 36 out of 96 tags, even where those tags shared less than 50% **homology**. The remaining 60 tagged plasmids were selected to carry out transformation experiments individually. We subsequently demonstrated that oligonucleotide tags from mutants of *D. desulfuricans* and *S. oneidensis* can be amplified directly from chromosomal DNA and screened with microarrays for use in identification of genes required for survival of microorganisms in their natural environment.

L16 ANSWER 124 OF 157 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2002:241116 CAPLUS
 DOCUMENT NUMBER: 136:258302
 TITLE: Phylogenetic tree diagram **display** for gene expression data cluster analysis
 INVENTOR(S): Nozaki, Yasuyuki; Nakashige, Ryo; Tamura, Takuro
 PATENT ASSIGNEE(S): Hitachi Software Engineering Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002025489 W: JP, US RW: DE, FR, GB	A1	20020328	WO 2000-JP6385	20000919
EP 1321858 R: DE, FR, GB	A1	20030625	EP 2000-961085	20000919
JP 3532911	B2	20040531	JP 2002-529422 WO 2000-JP6385	20000919 W 20000919

PRIORITY APPLN. INFO.: AB A system of cluster anal. for gene expression data from DNA **microarray hybridization** is described that uses standard statistical algorithms to arrange genes according to **similarity** in pattern of gene expression. The output is **displayed** graphically, in the form of phylogenetic tree diagram, conveying the clustering and the underlying expression data simultaneously in a form intuitive for biologists. A threshold indicating a **similarity** of expression patters is preset, and genes with the same function and genes similar in expression pattern to those genes are extracted and **displayed**. In addition, an experiment pattern required by clustering is reselected for the extracted genes and is then used to subject them to cluster anal. How many individual functions are available in genes belonging to a partial tree is calculated to determine ratios in which individual functions account for in a partial tree. If their ratios in the partial tree exceed the preset threshold, they are regarded as a cluster (set of genes similar

in function) and are subjected to extraction processing.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 139 OF 157 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2001-09306 BIOTECHDS

TITLE: A method **visualizing** relationships in data sets
using arrays;

DNA **microarray**, DNA chip, database and computer
program for sequence **homology** detection and
bioinformatics

AUTHOR: van der Krieken W M; Kodde J

PATENT ASSIGNEE: Plant-Research-International

LOCATION: Wageningen, The Netherlands.

PATENT INFO: WO 2001027809 19 Apr 2001

APPLICATION INFO: WO 2000-NL742 16 Oct 2000

PRIORITY INFO: NL 1999-13297 15 Oct 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-273864 [28]

AN 2001-09306 BIOTECHDS

AB A method of comparing and/or analyzing databases, such as databases obtained in one or more DNA array (preferably databases originating from DNA microarrays and DNA chips) forms or in a matrix form is claimed. The data and relations from the DNA arrays or matrices with mutual correlations are placed via arrangement in a virtual matrix, where these mutual relations or correlations can be made easily visible for a user, for instance on a screen. Also claimed are: a computer system, in which a program is stored to perform the method; and a database obtained according to the method. The method is useful for comparing and analyzing databases in a DNA array or matrix form. The method provides for effortless comparison between two or more data sets, to reveal differences and/or similarities. The technique has importance for comparison of DNA microarrays, especially in view of their potentially large number of members. All kinds of files of dot blots can be analyzed. Application to e.g. cDNA-AFLP, RNA Northern **hybridization**, Southern **hybridization** and protein arrays from proteomics. (34pp)

L16 ANSWER 141 OF 157 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:703609 CAPLUS

DOCUMENT NUMBER: 135:252753

TITLE: **Hybridization** experiment result
display method

INVENTOR(S): Tamura, Takuo; Yamamoto, Nobuyuki; Suzuki, Nobuaki;
Mizuno, Katsuya

PATENT ASSIGNEE(S): Hitachi Software Engineering Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 2001264330	A2	20010926	JP 2000-70915	20000314
PRIORITY APPLN. INFO.:			JP 2000-70915	20000314

AB A method for **displaying** the **hybridization** experiment result is provided, which verifies the accuracy of the experiment Upon **displaying** the exptl. result on the **hybridization** between multiple probe biomacromols. immobilized on a **biochip** and a sample biomacromol., the **homol.** score indicating the **homol.** degree in the base sequence between each probe biomacromol.

is **displayed** together with the information on the **hybridization** quantity at each probe biomacromol. obtained by the **hybridization** experiment. Diagrams describing the **display** method are given.

=>

method **visualizing** relationships in data sets
using arrays;
DNA **microarray**, DNA chip, database and computer
program for sequence **homology** detection and
bioinformatics

AUTHOR: van der Krieken W M; Kodde J
PATENT ASSIGNEE: Plant-Research-International
LOCATION: Wageningen, The Netherlands.
PATENT INFO: WO 2001027809 19 Apr 2001
APPLICATION INFO: WO 2000-NL742 16 Oct 2000
PRIORITY INFO: NL 1999-13297 15 Oct 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-273864 [28]
AN 2001-09306 BIOTECHDS

AB A method of comparing and/or analyzing databases, such as databases obtained in one or more DNA array (preferably databases originating from DNA microarrays and DNA chips) forms or in a matrix form is claimed. The data and relations from the DNA arrays or matrices with mutual correlations are placed via arrangement in a virtual matrix, where these mutual relations or correlations can be made easily visible for a user, for instance on a screen. Also claimed are: a computer system, in which a program is stored to perform the method; and a database obtained according to the method. The method is useful for comparing and analyzing databases in a DNA array or matrix form. The method provides for effortless comparison between two or more data sets, to reveal differences and/or similarities. The technique has importance for comparison of DNA microarrays, especially in view of their potentially large number of members. All kinds of files of dot blots can be analyzed. Application to e.g. cDNA-AFLP, RNA Northern **hybridization**, Southern **hybridization** and protein arrays from proteomics. (34pp)

enome-wide expression profiling of mid-gestation placenta
and embryo using a 15,000 mouse developmental cDNA
microarray.

AUTHOR: Tanaka T S; Jaradat S A; Lim M K; Kargul G J; Wang X;
Grafovac M J; Pantano S; Sano Y; Piao Y; Nagaraja R; Doi H;
Wood W H 3rd; Becker K G; Ko M S

CORPORATE SOURCE: Laboratory of Genetics and DNA Array Unit, National
Institute on Aging, National Institutes of Health,
Baltimore, MD 21224-6820, USA.

SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (2000 Aug 1) 97 (16) 9127-32.
Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-AW537829; GENBANK-AW537830; GENBANK-AW537831;
GENBANK-AW537832; GENBANK-AW537833; GENBANK-AW537834;
GENBANK-AW537835; GENBANK-AW537836; GENBANK-AW537837;
GENBANK-AW537838; GENBANK-AW537839; GENBANK-AW537840;
GENBANK-AW537841; GENBANK-AW537842; GENBANK-AW537843;
GENBANK-AW537844; GENBANK-AW537845; GENBANK-AW537846;
GENBANK-AW537847; GENBANK-AW537848; GENBANK-AW537849;
GENBANK-AW537850; GENBANK-AW537851; GENBANK-AW537852;
GENBANK-AW537853; GENBANK-AW537854; GENBANK-AW537855;
GENBANK-AW537856; GENBANK-AW537857; GENBANK-AW537858; +
200009

ENTRY MONTH: Entered STN: 20000915

ENTRY DATE: Last Updated on STN: 20000915
Entered Medline: 20000905

AB cDNA **microarray** technology has been increasingly used to monitor global gene expression patterns in various tissues and cell types. However, applications to mammalian development have been hampered by the lack of appropriate cDNA collections, particularly for early developmental stages. To overcome this problem, a PCR-based cDNA library construction method was used to derive 52,374 expressed sequence tags from pre- and peri-implantation embryos, embryonic day (E) 12.5 female gonad/mesonephros, and newborn ovary. From these cDNA collections, a **microarray** representing 15,264 unique genes (78% novel and 22% known) was assembled. In initial applications, the divergence of placental and embryonic gene expression profiles was assessed. At stage E12.5 of development, based on triplicate experiments, 720 genes (6.5%) **displayed statistically significant differences in expression between placenta and embryo**. Among 289 more highly expressed in placenta, 61 placenta-specific genes encoded, for example, a novel prolactin-like protein. The number of genes highly expressed (and frequently specific) for placenta has thereby been increased 5-fold over the total previously reported, illustrating the potential of the **microarrays for tissue-specific gene discovery and analysis of mammalian developmental programs**.

L20 ANSWER 7 OF 7 MEDLINE on STN
ACCESSION NUMBER: 1999061959 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9843981
TITLE: Cluster analysis and **display** of genome-wide expression patterns.
AUTHOR: Eisen M B; Spellman P T; Brown P O; Botstein D
CORPORATE SOURCE: Department of Genetics, Stanford University School of Medicine, 300 Pasteur Avenue, Stanford, CA 94305, USA.
CONTRACT NUMBER: CA46406 (NCI)
CA77097 (NCI)
HG00983 (NHGRI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1998 Dec 8) 95 (25) 14863-8.

PUB. COUNTRY: Journal code: 7505876. ISSN: 0027-8424.
United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 20000303
Entered Medline: 19990114

AB A system of cluster analysis for genome-wide expression data from DNA **microarray hybridization** is described that uses standard **statistical** algorithms to arrange genes according to **similarity** in pattern of gene expression. The output is **displayed** graphically, conveying the clustering and the underlying expression data simultaneously in a form intuitive for biologists. We have found in the budding yeast *Saccharomyces cerevisiae* that clustering gene expression data groups together efficiently genes of known similar function, and we find a similar tendency in human data. Thus patterns seen in genome-wide expression experiments can be interpreted as indications of the status of cellular processes. Also, coexpression of genes of known function with poorly characterized or novel genes may provide a simple means of gaining leads to the functions of many genes for which information is not available currently.

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Phylogenetic tree diagram **display** for gene expression data cluster analysis
INVENTOR(S) : Nozaki, Yasuyuki; Nakashige, Ryo; Tamura, Takuro
PATENT ASSIGNEE(S) : Hitachi Software Engineering Co., Ltd., Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002025489 W: JP, US RW: DE, FR, GB	A1	20020328	WO 2000-JP6385	20000919
EP 1321858 R: DE, FR, GB	A1	20030625	EP 2000-961085	20000919
JP 3532911	B2	20040531	JP 2002-529422 WO 2000-JP6385	20000919 W 20000919

PRIORITY APPLN. INFO.:

AB A system of cluster anal. for gene expression data from DNA **microarray hybridization** is described that uses standard statistical algorithms to arrange genes according to **similarity** in pattern of gene expression. The output is **displayed graphically**, in the form of phylogenetic tree diagram, conveying the clustering and the underlying expression data simultaneously in a form intuitive for biologists. A threshold indicating a **similarity** of expression patters is preset, and genes with the same function and genes similar in expression pattern to those genes are extracted and **displayed**. In addition, an experiment pattern required by clustering is reselected for the extracted genes and is then used to subject them to cluster anal. How many individual functions are available in genes belonging to a partial tree is calculated to determine ratios in which individual functions account for in a partial tree. If their ratios in the partial tree exceed the preset threshold, they are regarded as a cluster (set of genes similar in function) and are subjected to extraction processing.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 8 MEDLINE on STN
ACCESSION NUMBER: 1999061959 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9843981
TITLE: Cluster analysis and **display** of genome-wide expression patterns.
AUTHOR: Eisen M B; Spellman P T; Brown P O; Botstein D
CORPORATE SOURCE: Department of Genetics, Stanford University School of Medicine, 300 Pasteur Avenue, Stanford, CA 94305, USA.
CONTRACT NUMBER: CA46406 (NCI)
CA77097 (NCI)
HG00983 (NHGRI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1998 Dec 8) 95 (25) 14863-8.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 20000303
Entered Medline: 19990114

AB A system of cluster analysis for genome-wide expression data from DNA **microarray hybridization** is described that uses standard statistical algorithms to arrange genes according to **similarity**

in pattern of gene expression. The output is **displayed graphically**, conveying the clustering and the underlying expression data simultaneously in a form intuitive for biologists. We have found in the budding yeast *Saccharomyces cerevisiae* that clustering gene expression data groups together efficiently genes of known similar function, and we find a similar tendency in human data. Thus patterns seen in genome-wide expression experiments can be interpreted as indications of the status of cellular processes. Also, coexpression of genes of known function with poorly characterized or novel genes may provide a simple means of gaining leads to the functions of many genes for which information is not available currently.

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1999061959 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9843981
TITLE: Cluster analysis and **display** of genome-wide expression patterns.
AUTHOR: Eisen M B; Spellman P T; Brown P O; Botstein D
CORPORATE SOURCE: Department of Genetics, Stanford University School of Medicine, 300 Pasteur Avenue, Stanford, CA 94305, USA.
CONTRACT NUMBER: CA46406 (NCI)
CA77097 (NCI)
HG00983 (NHGRI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1998 Dec 8) 95 (25) 14863-8.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 20000303
Entered Medline: 19990114
AB A system of cluster analysis for genome-wide expression data from DNA **microarray hybridization** is described that uses standard statistical algorithms to arrange genes according to **similarity** in pattern of gene expression. The output is **displayed graphically**, conveying the clustering and the underlying expression data simultaneously in a form intuitive for biologists. We have found in the budding yeast *Saccharomyces cerevisiae* that clustering gene expression data groups together efficiently genes of known similar function, and we find a similar tendency in human data. Thus patterns seen in genome-wide expression experiments can be interpreted as indications of the status of cellular processes. Also, coexpression of genes of known function with poorly characterized or novel genes may provide a simple means of gaining leads to the functions of many genes for which information is not available currently.

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